FROM BIOMETRIKA, A JOURNAL FOR THE STATISTICAL STUDY OF BIOLOGICAL PROBLEMS VOL. VII. NO. 3, APRIL 1910

19.

# HISTOLOGICAL EXAMINATION OF A CASE OF ALBINISM

BY

J. E. ADLER, F.R.C.S. AND J. McINTOSH, M.D.

CAMBRIDGE
AT THE UNIVERSITY PRESS
LONDON: FETTER LANE, C. F. CLAY, MANAGER
AND H. K. LEWIS, GOWER STREET
EDINBURGH: 100, PRINCES STREET
BERLIN: A. ASHER AND CO.
LEIPSIC: BROCKHAUS
NEW YORK: G. P. PUTNAM'S SONS
BOMBAY AND CALCUTTA: MACMILLAN AND CO., LIMITED

[*From Biometrika, Vol. VII. No.* 3. *April,* 1910.]

[*All Rights reserved.*]

# HISTOLOGICAL EXAMINATION OF A CASE OF ALBINISM.

By J. E. ADLER, F.R.C.S. and J. M<sup>c</sup>INTOSH, M.D.

(*From the Bacteriological Laboratory, London Hospital, E.*)

Albinism has now long been a subject of interest to medical science, and many papers have appeared from time to time descriptive of its clinical peculiarities. The literature on the histological findings of the affected parts is, however, most scanty, and is usually confined to descriptions of pieces of the iris removed at operations for traumatic and other affections.

In looking through the literature only one record of a complete post-mortem examination on an albino could be found. This was made by Buzzi in 1783 (2). The case from his description appears to have been a complete albino, but his descriptions of the minute anatomy are far from satisfactory. Carron du Villards (1) and Maury (8) record dissections of human albino eyes; the former with absence of all pigment, the latter with traces of pigment.

It is a pity that a more uniform system of classification has not been adopted by the various observers in the description of their cases, so that it might have been possible to get a correct idea of the condition observed.

All the cases on which histological observations have been made, with the exception of Buzzi's case, would come under the groups of incomplete albinism, according to the classification proposed by Geoffroy Saint Hilaire (3).

In the case of partial albinism recorded by Mueller (9), there was a complete absence of all pigment in certain areas of the iris. In Nettleship's case there was a complete absence of pigment in the portion of the iris examined which was probably a fair sample. On the other hand, in Usher's cases of incomplete albinism recorded by Nettleship (10), there was diminished pigment in both choroid and retina. Clinically Usher's cases might pass for complete albinos, and this would mean that we could not distinguish by clinical methods between cases of incomplete and complete albinism.

The case with which we are about to deal, and which we had the opportunity of examining, was that of a female child of 10 weeks. The child was the second albino in the family, and the mother had taken the matter so much to heart that she committed suicide. She left the child exposed, and from the effects of this it died.

*Family History.* The family history of the child was specially investigated in order to ascertain whether there was a hereditary history of albinism; but no evidence of albinism could be found in any of the ancestors or relations in the four previous generations. The description of the family tree (see p. 243) connected with the case is as follows (unless marked as albino, all members are normal):—

Generation IV. 12. B. C., aet. 10, albino—pink eyes, nystagmus, white hair, big healthy boy, very bright. 13. L. C., aet. 8, ♂ healthy. 14. —. C., aet. 6, ♀ healthy. 15. N., aet. 4, ♂. 16. O. C., aet. 3, ♀ healthy. 17. C. C., aet. 6 weeks, ♀ albino, the case described. IV. 1. S. W., aet. 25, ♂ healthy. 2. L. W., aet. 24, ♂ healthy. 3. E. W., aet. 22, ♀ healthy. 4. B. W., aet. 22, ♀. 5. P. K., aet.?, ♂. 6. A. K., aet.?, ♀. 7. G. D., aet. 13, ♂. 8. D. E., aet. 8, ♂. 9. J. E., aet. 9, ♂. 10. S. E., aet. 10, ♀. 11. M. E., aet. 11, ♀. 18. B. S., aet. 9, ♂. 19. D. S., aet. 7½, ♀.

Generation III. 1. R. W., father of family IV. 1—4. 2. M. A. W., wife of III. 1, healthy (eldest sister). 3. A. K., sister of III., 2. 4. P. K., her husband, father of family IV. 5—6. 5. L. C., mother of IV. 7, and wife of III. 6. 6. G. D., husband. 7. L. C., ♀, died. 8. E. C., ♀, died. 9. D. C., ♂, married to III. 10. 10. S. E., ♀, became wife of III. 9, mother of IV. 8—11. 11. A. C., ♂, died. 12. A. C., ♂, youngest child, father of case, married III. 27 (L. R.), alive. 13—17, Children of W. C., II. 3—4, all unaffected, but all details unknown. 18, 19, 20, and 21, Children of A. C., II. 5—6, all unaffected, details unknown. 22. A. R., ♀, spinster, pale, but not a true albino. 23. F. R., ♀. 24. G. R., ♂, in asylum. 25. H. R., ♂, married D. S., ♀, III. 26. ♀, wife of IV. 18, 19. 27. ♀, L. R., married A. C., III. 11, died examined, found unaffected, mother of the two albinos in the family. 28. ♂, S. R., just married to III. 29. ♀. 30. ♀, P. R., just married to III. 31. ♂, B. 32. If any, and how many, unknown. 33—34. Offspring of II. 11 and 12, age and sex unknown, known however to be normal. 35. If any, no details known. 36—45. Offspring of II. 15—16, all unaffected, but no details as to order and sex.

Generation II. 1. D. C., alive, ♂, aet. 74, unaffected. 2. M. A. S., ♀, wife of above, unaffected, parents of III. 1—12. 3. W. C., ♂, died, age unknown, unaffected. 4. ♀, his wife, unaffected. 5. A. C., ♂, died, age unknown, unaffected. 6. ♀, his wife, unaffected. 7. A. C., ♀, married G. R. (8), ♂, parents of family III. 22—30. 9. S. C., ♀, married 10. ♂, age and initials unknown. 11. L. C., ♀, married 12, ♂, age and initials unknown. 13. A. C., ♀, married 14, ♂, age and initials unknown. 15. M. C., ♀, married 16, ♂, age and initials unknown; II. 15—16 parents of III. 36—45. 17. ♀, sister of G. R., II. 8, unaffected. 18. ♀, sister of G. R., II. 8, unaffected. 19. ♀, sister of G. R., II. 8, unaffected.

Generation I. 1. D. C., ♂, died, aet. 72, unaffected. 2. ♀, wife of above, unaffected, all other details unknown. 3. R., ♂, unaffected, all details unknown. 4. ♀, unaffected.

## *Pathological Anatomy—Post-mortem Notes.*

*External Appearances.* The body was that of a well nourished female child of about six weeks. Rigor mortis was absent.

There were small papular erythematous patches on the extensor aspects of both wrists, forearms and legs; symmetrically arranged ecchymoses were seen on the upper and inner aspects of both thighs.

The back, shoulders, and sides were covered with fine white downy hairs. The nipple, umbilicus, perineum, and anus were unpigmented. The scalp was covered with a large quantity of fine silky hair about an inch long. No hairs were pigmented. The eyebrows consisted of white hairs, while the eyelashes were regular, even, and white.

The eyes were pink; the pupils equal, and moderately small. The irides were entirely devoid of all pigment, and were pinkish in colour, with fine greyish white radially arranged striations.

Weight, 7 lbs. 14 ozs. Circumference of head, $14\frac{1}{2}$ ins.

On opening the thorax, the thymus gland was found to be enlarged, and reached down as far as the level of the third costal cartilage; weight, $\frac{1}{2}$ oz. There was no excess of fluid in either pleural cavity, and there were no pleuritic adhesions. The lungs were collapsed, definite capillary bronchitis being present. The mucous membrane of the bronchi was congested, and the larger bronchi contained some yellowish pus. There was no consolidation. Weight, right lung, $1\frac{1}{4}$ ozs.; left lung, $1\frac{3}{4}$ ozs.

*The Heart.* There was no excess of fluid in the pericardium. The foramen ovale was not completely closed, and admitted a fine probe. The valves and aorta were normal in appearance. Weight, $\frac{3}{4}$ oz.

*The Stomach.* The stomach was almost empty, and very pale in colour; two or three ecchymotic spots were noticed on its anterior surface near the greater curvature. The stomach contained about two or three drachms of mucous fluid, which was odourless. The mucous membrane appeared healthy.

*The Liver* protruded one finger's breadth below the costal margin, and, on being cut into, appeared to be normal. No thickening of the capsule was noticed. The gall bladder was filled with the usual yellow bile, and the ducts were found patent.

*The Spleen* ($\frac{1}{4}$ oz. in weight) was firm in texture. On section, the malpighian bodies were not distinctly marked.

*The Kidneys* ($\frac{1}{4}$ oz. each in weight) were lobulated. Their capsule stripped readily, and the perirenal fat was plentiful and normal in colour. The ureters were patent, and were followed into the bladder. The latter was empty, and was healthy in appearance. Both suprarenal glands were present, and appeared normal.

The small intestine was, for the most part, thin and empty, and the mucous membrane, though pale in colour throughout, appeared to be healthy; while the Peyer's patches presented a normal appearance. The large intestine, appendix, and rectum were examined and found to be healthy. The pancreas appeared to be normal, both in regard to structure and weight; the duct of Wirsung was patent. The mesenteric, bronchial, cervical, and axillary glands were normal in size, and presented the usual appearance on section. The tongue, tonsils, and oesophagus were normal. The uterus and cervix were infantile in shape, but the ovaries were both enlarged and cystic. Pieces were removed from each organ, and placed in a solution of formalin (1 in 10) for histological examination.

*The Brain* was removed intact (weight, 1 lb. ½ oz.), and was very soft. The dura mater, as is usual in children, was adherent at the suture lines. The cerebral sinuses were found to be normal. The pituitary body with the sella turcica appeared to be normal, and were removed en masse.

*Histopathology.* All the organs and tissues were examined microscopically, but, apart from a complete absence of any pigment in certain parts, no histological peculiarities were observed. With regard to the liver, spleen, lungs, kidneys, pancreas, thymus, thyroid, heart, and muscles, no abnormality was made out; while in the other structures, namely, brain, eyes, internal ear, suprarenal gland, skin, and hair, the only noticeable feature was a complete absence of pigment.

*Brain.* Sections of the cerebrum, cerebellum, crura cerebri, pons Varolii, and medulla oblongata were examined, both in the stained and unstained condition. Search was made for pigment in those parts in which pigmentation normally exists in the brain cells in the adult. The various nuclei of the pons, medulla, and cerebellum, the substantia nigra and the grey matter were examined, but contained no pigment granules.

Sections of these areas were also stained with fluorescein, but no granules were found.

The pituitary body was apparently normal in structure.

*The Eyes.* Both eyes were examined completely; one was fixed in formalin (10 °/₀) and the other in spirit, and then they were frozen solid and cut into right and left halves. The internal aspect of the eyeballs was like yellowish white parchment. The vessels were clearly outlined on their surface, while the fovea centralis appeared as a distinct spot of a slightly deeper tint than the surrounding retina.

Paraffin and celloidin sections were made and examined under the microscope by day and artificial light, without even a trace of pigment being found in any of the structures of the eye, whether of an ectodermic or mesodermic origin, retina, epithelium and stroma of iris or choroid : see Plate II.

Owing to the entire absence of pigment in the eyes, the anatomical structure of the irides and retina was shown to great advantage, while the arrangement of the delicate connective tissue of the iris and its continuity with the choroid and ciliary processes were clearly seen. The arrangement of the two sets of muscle fibres could be followed. The iris also showed a well-marked crypt. Unfortunately the retina had not been fixed soon enough after death to preserve the rods and cones layer intact, their situation however can be easily recognised.

The choroid and retina were examined in the stained and unstained condition.

*Internal Ear.* The petrous portion of the temporal bone containing the middle and internal auditory apparatus was removed entire and decalcified. The internal ear contained no pigment in the mesoblastic cells of the perilymphatic spaces.

*The Suprarenal Gland.* The medulla and the cortex appeared to be of the usual proportions; no brown granules were to be observed in those cells of the cortex which are usually found to contain pigment in adult life.

*The Skin.* Except for the absence of pigment, the only noticeable feature seen in sections of the skin was the non-granular appearance of the rete mucosum.

*The Hair* contained no pigment; after the hairs were cleared in xylol they became quite transparent, and could be seen only with considerable difficulty.

In conclusion, one must say that the case described above is one of complete albinism, on account of the complete absence of any melanin pigment in those structures which normally contain it.

This child, though it might also be described in Professor Karl Pearson's terminology as an internal albino, does not solve the question as to whether internal albinism exists in adult albinos, because practically no pigment exists in any part of the brain of a child before the sixth month of life (Marinesco (7)). The same is also true for those glands, such as the suprarenal, which contain pigment in adult life (Koelliker (5)).

There was no evidence of any maldevelopment or mental feebleness in any member of the family, such as has been reported in certain albinotic stocks. But though there is undoubted proof that in certain instances deficiency of pigment does go along with such conditions, we have no reason to suppose that there is a constant relation between them.

In all probability this child, had it lived, would have remained a complete albino even in spite of the fact that the colour of the iris in all infants darkens considerably during the first year of life, because it is very unlikely that pigmentation would occur after so long a period of complete absence, namely, over 10 months, as melanin pigment, according to Koelliker (4), makes its appearance in the retina towards the fourth week of intra-uterine life. The specimens kindly lent by Dr Low (6) showed distinct pigment in the retina at this period: see Plate I.

Where the albinism entered this family is not at all clear; if the condition is not a sport it is most likely that the condition was handed down from the (paternal) grand-parents, as the parents of the child were cousins. From a Mendelian view both parents might be described as carrying recessive albinism, but we have really no evidence from this single case to support this view.

## BIBLIOGRAPHY.

(1) Carron du Villards. Bulletin Médicale Belge, p. 61, March, 1838.

(2) Buzzi, Del Sig. Francesco. Dissertazione storico-anatomica, sopra una varietà particolare d' Uomini bianchi Eliofobi. Chirurgo-Oculista ed Aiutante Chirurgo nell' Ospedale Maggiore di Milano, 1783.

(3) Geoffroy Saint Hilaire. De l'Albinisme; histoire générale et particulare des anomalies de l'organisation, T. 1, 1832.

(4) Koelliker. Entwicklungsgeschichte des Menschen und der höheren Thiere, Leipzig, 1861.

(5) ——. Handbuch der Gewebelehre des Menschen, Bd. iii., S. 391, Leipzig, 1899.

(6) Low, A. Personal communication.

(7) Marinesco. La Cellule Nerveuse, Paris, 1909, T. 1, p. 277.

(8) Maury. Archiv für Ophthalmologie, Bd. xxiv., Ab. iv., S. 139, Berlin, 1878.

(9) Mueller, (L.). Ueber eine neue Anomalie der Iris. Beiträge zur Augenh., Bd. vii., p. 88, Leipzig, 1892.

(10) Nettleship. Cases and Observations. Roy. London Ophth. Hosp. Reports, Vol. xv., p. 110, 1902, and Trans. Ophth. Soc., Vol. xxvi., p. 244 (with plate), 1906.

## DESCRIPTION OF PLATES.

Plate I. Fig. 1. Section of Eye in 4th week embryo.
Fig. 2. Section of Eye in 10th week foetus.

We owe these sections to the kindness of Dr A. Low.

Plate II. Fig. 3. Section of retina of albino case.
Fig. 4. Section of retina of normal infant.
Fig. 5. Section of iris of albino case.
Fig. 6. Section of iris from normal infant.

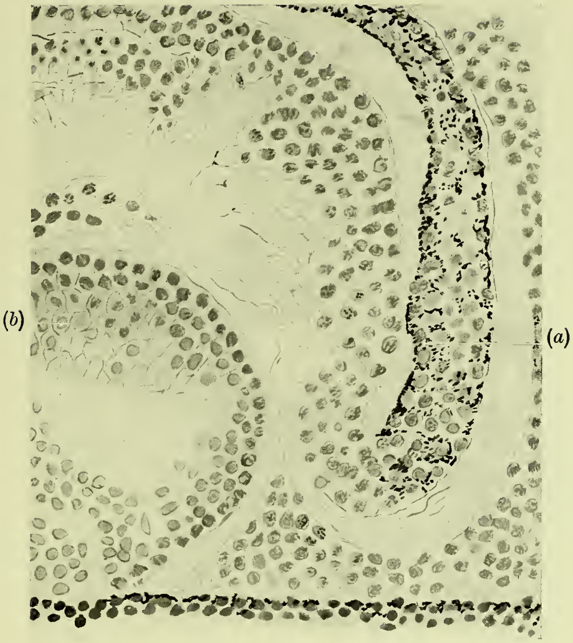


Fig. 1. Section of eye in 4th week embryo (10 mm. long).

(a) Pigment granules in pigment layer of retina.

(b) Lens.

[Dr Low's section]

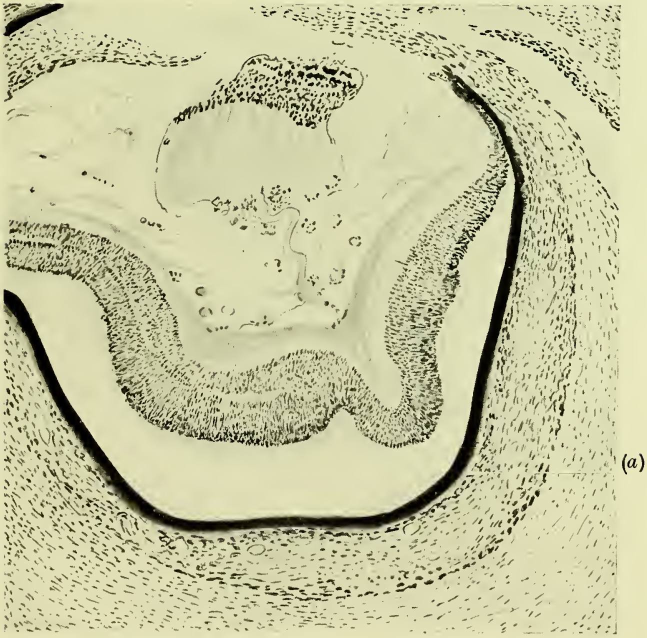


Fig. 2. Section of eye, 10th week foetus (28 mm. long).

(a) Pigment layer of retina.

[Dr Low's section]

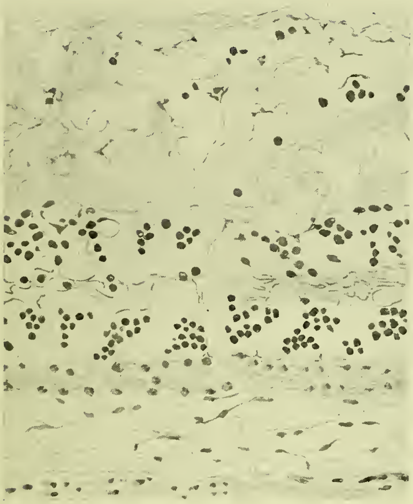


FIG. 3. Section of retina of albino child, with absence of all pigment.

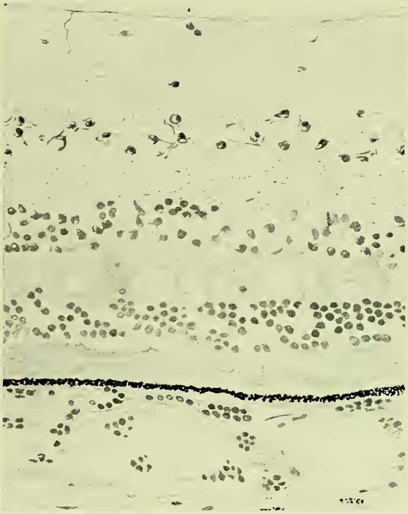


FIG. 4. Section of retina of normal child of same age, showing pigment layer.

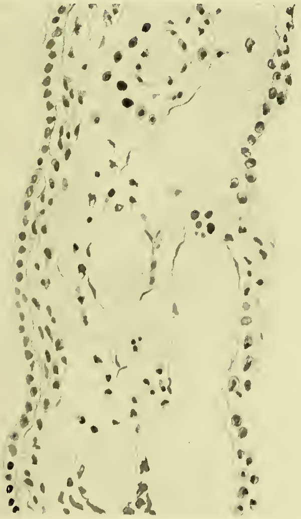


FIG. 5. Section of iris of albino child, with absence of all pigment.

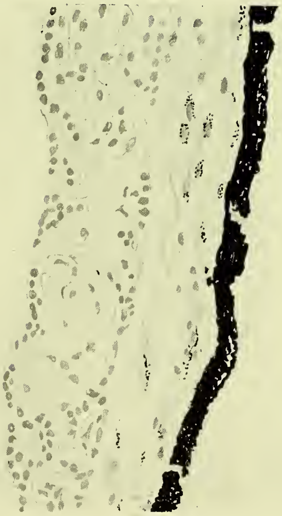
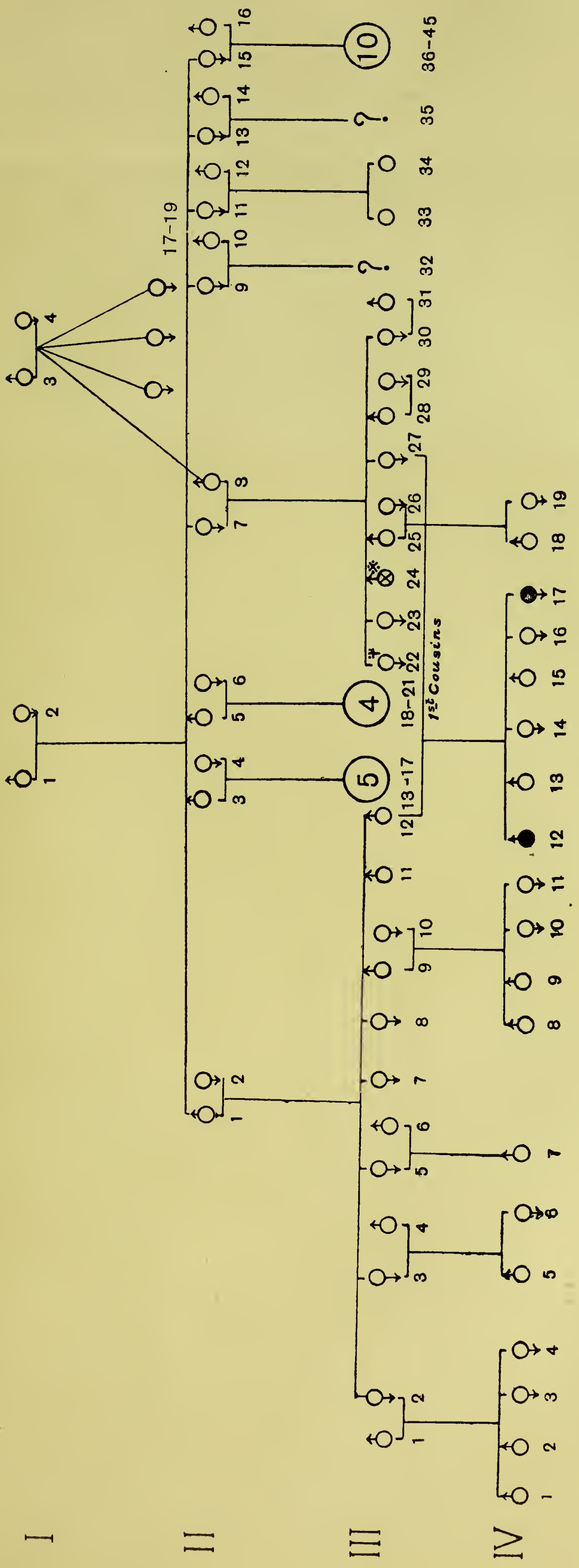


FIG. 6. Section of iris from normal child of same age.



* In an asylum.

# BIOMETRIKA

This Journal appears about four times a year, and is devoted to the Statistical Study of Biological Problems. A volume containing about 500 pages, with plates and tables, is issued annually.

Papers for publication should be sent to Professor Karl Pearson, University College, London. It is very desirable that a copy of all measurements made, not necessarily for publication, should accompany each paper. In all cases the papers themselves should contain not only the calculated constants, but the distributions from which they have been deduced. Diagrams and drawings should be sent in a state suitable for direct photographic reproduction, and if on decimal paper, it should be *blue* ruled, and the lettering only pencilled.

Books and offprints for review or notice in the bibliography should be sent to Prof. Pearson, University College, London, and, when a second copy is available, to Dr Raymond Pearl, Maine Agricultural Experiment Station, Orono, Maine, U.S.A.

Papers will be accepted in German, French or Italian. In the first case the manuscript should be in Roman not German characters.

Contributors receive 25 copies of their papers free. Twenty-five or fifty additional copies may be had on payment of 3/6 or 6/- respectively per sheet of eight pages: these should be ordered when the final proof is returned.

All communications, other than those relating to contributions or publications for review, should be addressed to the University Press, Cambridge.

The subscription price, payable in advance, is 30*s. net* per volume (post free), single numbers 10*s. net.* Volumes I, II, III, IV, V and VI (1902—9) complete, 30*s. net* per volume. Bound in Buckram 34/6 *net* per volume. Index to Volumes I to V 2*s. net.* Subscriptions may be sent to C. F. Clay, Manager, Cambridge University Press, Fetter Lane, London, E.C., either direct or through any bookseller.